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09/742,520	12/20/2000	Ilham Saleh Abuljadayel	674528-2001.2	9656

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EXAMINER
SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
742,526	ABULJADAYEL
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 11/21/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☐ Claim(s) 47-65 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 47-65 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 6

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

The amendment of 11/12/01 (Paper 7) has been entered. Claims 47-65 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's response has overcome the previously stated rejections, under 112, second paragraph.

Applicant's response regarding the 112, first paragraph rejections of record has been considered. The examiner has withdrawn the 112, first paragraph scope of enablement rejection, as it pertains to limiting the invention to use of human cells. With respect to respect to the scope of enablement rejection pertaining to limiting the invention to use of anti-HLA-DR beta chain antibodies, see comments further below.

Claims 47-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is claiming new matter in claim 47 by reciting a method of increasing the relative number of CD45 low cells.

The examiner notes that page 28 of the specification teaches that treatment of peripheral blood samples with antibody to the HLA-DR beta chain increases the relative number of CD45 low cells. However, at most, this passage of the specification merely notes this increase as an interesting observation pertaining to the expression of a particular antigen present on all human

leukocytes. This passage, as well as the Summary of the Invention" (pages 6-18) and the Summary (pages 39-42), fail to point out that the CD45-lo population is of any particular interest for one to prepare. The examiner can only find teachings of CD34+ undifferentiated cells and CD19+ and CD3+ redifferentiated cells in the Summary of the Invention. Applicant's written specification, Tables, and Charts refer to numerous observations pertaining to the increase or decrease in a variety of CD antigens, following incubations of peripheral blood cells with various agents and under various conditions. However nothing in the disclosure points the reader to the CD45 low population as being of particular interest. Since one would not have been led to consider this particular cell population, applicant was not in possession of the invention at the time of filing. Relevant case law is found in In Re Ruschig 154 USPQ 118.

Other new matter issues pertaining to the rejected claims are as follows:

In claim 48, the examiner finds no basis for reciting that the agent "engages a receptor that mediates, capture recognition or presentation of an antigen at the surface". In the description at pages 11-13, the examiner cannot find this functional language; the examiner only finds mention of MHC class I and II. Applicant has therefore entered new matter by reciting a new subgenus of agents encompassing more than MHC class I and II receptors.

In claim 49 "2 to 24 hours" is new matter. The examiner cannot find this range recited in the original disclosure.

In claim 52, the examiner finds no disclosure support for reciting that CD45+ committed cells include the variously recited colony forming cells. At page 28, applicant only disclosed B and T cells, among those recited in claim 52, as expressing CD45.

For claim 53, the examiner fails to find any teaching at pages 28-29 that the detected population of CD45 low cells is MHC class I+ or class II+.

Claims 47-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant was not in possession of the genus of agents that operably engage committed cells, nor of the genus of "biological response modifiers".

Applicant has defined the agent as one that "operably engages a more committed cell to retro differentiation" (page 11). This is merely a statement of a desired function and not a description of what distinguishes the genus of such agents from compounds which are not. Applicant has not even defined what is encompassed by the term "operably engages", e.g. as to whether it encompass only binding of the agent to a receptor or whether it also encompasses interaction of the agent with mediators that operate "downstream" of the receptor, e.g. with members of a signal transduction pathway. Since applicant contemplates agents that interact on both the cell surface (page 11) and intracellularly (page 13), the Office interprets the term "operably engages" broadly. Applicant's disclosure however has given no direction as to what the agent is, except in the broadest sense as one that engages (binds?) a cell surface receptor.

Applicant gives various examples of such at page 12, lines 1-4, including such diverse agents as CAMP (which does not bind a cell surface receptor), CD 8, CD4, a TCR, ligand (binding what is not defined), peptide (doing what is not defined), and various types of antibodies (binding what is not defined). Applicant then continues by suggesting an agent that is an antibody to the alpha or beta chains of MHC class I or II molecules. (Page 12, lines 6-12).

The various suggested agents such as cAMP, CD4, CD8, TCR, ligands, peptides and antibodies have no art recognized common structure or function. Apart from antibodies directed to the above noted MHC receptors, one would not be able to envision what agents properly belong within the genus and what compounds would not belong. The noted antibodies directed to MHC are not representative of the entire genus, or even of a substantial portion of the genus. The genus would encompass numerous undiscovered compounds which would not be envisioned. Applicant was therefore not in possession of the genus of agents that would "operably engage committed cells" at the time of filing. Note that a mere functional description of a genus does not constitute proper description under 112, first paragraph. Applicant is referred to the Revised Interein Written Description Guidelines Fed. Reg., vol. 64, No 244, pages 71427-71440, Dec. 21, 1999.

In like manner, applicant has not adequately shown that he was in possession of the genus of "biological response modifiers". While the term "biological response modifiers" (BRMs) is art known as encompassing "a wide spectrum of molecules that alter the immune response" (Cruse et al., page 37), applicant's disclosure at page 14 utterly fails to define what kind(s) of

biological response(s) are to be modified; also the BRMs contemplated page 14, lines 4-6) including immunomodulators, growth factors, cytokines, cell surface receptors, hormones (affecting what?), nucleic acids, nucleotide sequences (encoding what?), or peptides (doing what?) clearly encompasses far more than what one of skill would envision as being a BRM, according to the art recognized definition. Further, the one and only exemplified BRM is the alkylating agent, cyclophosphamide. This particular BRM fails to fall within any functional or structural grouping contemplated at page 14, lines 4-6, and is not representative of the genus. In the absence of a clear definition of what kind of "biological response" is to be modified and in the absence of defining what are the common functions and structural features of the agents contemplated at page 14, applicant has failed to show that he was in possession of the genus of "biological response modifiers". At the most one might envision the subgenus of "alkylating agents" as constituting a properly described genus.

Claims 47-61 and 63-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of agents which are antibodies directed to the alpha or beta chains of MHC class I or II receptors, does not reasonably provide enablement for of any agent that operably engages committed cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Applicant's listings of suggested agents at pages 11-13 sets forth no art recognized common functional or structural

features of the agents, other than the desired function of operably engaging committed cells to retro differentiate.

As noted supra in the 112, first, lack of possession rejection, applicant has merely defined these agents by a desired function. Since the process of causing CD45+ or other hematopoietic lineage committed cells to dedifferentiate/retro differentiate is not art conventional, and since the functions of various cell surface receptors are diverse applicant is inviting one to conduct undue experimentation to discover any agents, other than the above noted antiMHC antibodies, with which to practice the invention.

Applicant's urgings filed on 11/21/01 have been considered but are unconvincing that there is enablement for any method other than one that uses antibodies directed to the alpha or beta chains of MHC class I or II.

Regarding the fact that a previous examiner allowed chains of greater breath in Patent '625, the present examiner is not bound by that examiner's action. See In re Ruschig 154 USPQ 118.

Claim 63 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for use of a biological response modifier that is an alkylating agent, does not reasonably provide enablement for of any biological response modifier to induce retro differentiation of committed cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Inducing CD45+ or other hematopoietic lineage

committed cells to dedifferentiate/retro differentiate is not conventional in the art. In the absence of guidance as to what type of "biological response" is to be modified and in the absence of a clear teaching of possible BRMs (page 14) that have any art recognized common function or structure (see 112, first, each of possession rejection supra), applicant is inviting one to conduct undue experimentation to discover BRMs, other than alkylating agents, with which to practice the invention.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 47-65 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

As noted further supra, in the 112, first paragraph, new matter rejection, applicant did not specifically point to the CD45 low population of cells mentioned at pages 28-29 as being what he considered as his invention. Applicant failed to note that this particular cell population was of interest and failed to point out what particular utility/use this cell population would have. That is, among the many possible hematopoietic related disorders, cancers, etc. which one'(s) would one want to treat with CD45 low cells? If one wanted to obtain CD45 low cells, in order to redifferetiate them into more committed cells, what kinds of patients would one want to obtain blood cells from in order to prepare CD45 low cells? Since applicant did not point out why the CD45 low population is of particular interest,

compared to cells having low expression of others antigens characteristic of committed cells, and did not point out what one would particularly do with CD45 low cells, applicant has not disclosed a specific utility for the cells which would be obtained by his claimed method.

Claims 47-65 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

New 112, second paragraph rejections are stated as follows:

Claims 54-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 54 and its dependents, "the receptor" lacks antecedent basis in claim 47. Because of this fact the relationship of the recited MHC antigens in claims 54-62 and of the "antibody" in claims 60-62 to the "agent" of claim 47 is unclear.

While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "biological response modulator" in claims 63-65 are used by the claim to mean "a modulator of any biological response," while the accepted meaning is "a modulator of an immunological response."

Claims 57-59 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The HLA-DR receptor recited in claim 56 inherently has a beta chain with homologous regions. Therefore claims 57-59 fail to further limit claim 56.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 47-66 and 68-87 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,090,625. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and copending claims are claiming the same process, except for the recited population of cells that are increased.

It is noted that the instant and copending steps of contacting and incubating are precisely the same, are conducted for the same time (2-24 hr.), and are effected by the same agent (anti-

HLA-DR beta chain antibody) and the same BRM (cyclophosphamide). The instantly recited population of CD45 low cells apparently refers merely to an additional property of the CD34+ cells or of an intermediate cells on the "retro differentiation" pathway to the CD34+ cell population recited in the issued claims. In any event, a terminal disclaimer would be required so that any patent issuing from this application would remain with the same assignee as that of Patent 6,090,625. This is considered necessary, since any one practicing the claimed steps would not know which of the two patents is being infringed. It is also deemed that a terminal disclaimer is properly required, since no restriction between the instant and issued claims was ever stated during examination of the claims of Patent 6,090,625.

The claims remain allowable over the prior art of record.

This action is co-signed by the group director.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on M-F from 8:15 a.m. to 4:45 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

Feb. 11, 2002

Feb. 21, 2002

David A. Saunders

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